REMARKS

New Claim 42 finds support in the paragraph bridging pages 5 and 6 and at page 7 line 1 of the specification.

Having regard to the rejection of Claims 1, 3-5 and 10-19 over WO88/08708, it was and is the applicant's position that the language "so as to delay its activity for a predetermined period" does distinguish claimed formulation from sustained release compositions. "Its" in the wording of claim 1 refers back to that active compound. When it is stated that activity of such compound is delayed, the natural understanding is that there is a period in which no activity occurs. However, in order to try to expedite prosecution, Claim 1 has been amended to make this explicit. Support for the amendment is found throughout the specification from which it is clear that the purpose of the invention is to produce a composition and method that avoids cholinesterase inhibition during periods during which a patient is intended to sleep, see for example the paragraph bridging pages 1 and 2 and that bridging pages 6 and 7 of the specification.

The only relevant passage of WO 88/08708 is on page 25 where it is stated:

> If desired such capsules may be in the form of sustained release capsules wherein the main capsule contains microcapsules of active compound which release the contents over a period of several hours thereby maintaining a constant level of active compound in the patient's blood stream.

This is clearly not a teaching that there should be periods in which activity is minimized. The objective is a "constant level of active compound".

Precisely the opposite of the purpose of the present invention.

As discussed during the interview with the previous Examiner, the essence of the present invention is to minimize action by acetylcholinesterase inhibitors as specified in the claims during periods of desired sleep. As suggested by that Examiner, a declaration by the inventor was submitted previously explaining this. In that declaration it was pointed out in paragraph 3 that the difference between sustained release as used in the prior art and delayed release as used in the present invention was clear from a reading of the present application. The purpose of the invention is delay the activity of the acetylcholinesterase that is used for a period (see page 2 line 13 to 14) so as to prevent such activity at a time when such activity is undesired. It is particularly important that activity of the drug should be minimized during sleep. There is of course always a risk that some drug "leak" from any formulation. But the object of the delay in the present invention is that there should to the extent possible be a period of zero release so that during the period corresponding to sleep little or no cholinesterase inhibition occurs. This is the meaning of references to delayed release in the present application.

The current Examiner makes no comment on this, but it is submitted that there is a clear difference between a sustained release formulation, which is common for many drugs to try to achieve uniform dosing levels, and the inventive delayed release formulation of the present invention where the essence of the invention is to provide a formulation where there is a period without drug activity. It is therefore submitted that Claims 1, 3-5 and 10 - 19 meet the requirements of 35 USC 103. Nothing in WO88/08708 would lead one to produce a formulation in which there was such a period of no drug activity.

The Examiner has also rejected Claims 1, 3-5, 7-21, 22, 24-26, and 28-

41 under 35 USC 103(a).over the combination of WO88/08708 and Moorman U.S. 5,643, 905. The issues are similar to those discussed above namely whether the claims properly incorporate the "release avoidance concept".

As noted above, it is submitted that the use of the word "delay" accomplished this. However, in order to try to expedite prosecution, similar amendments to those made to Claim 1 have been made to independent Claim 21. Claim 41 has also been amended to emphasize the avoidance of release of inhibitor during a sleep period. It is submitted that these claims and those dependent on it now clearly set out the inventive difference from a combination of WO 88/08708 and Moorman. Neither of these teaches that a drug should be formulated such that there is a period during which drug activity is avoided as now set out in both of Claims 1 and 21 choosing both the manner of formulation and the half life of the drug in such a way as to provide for such periods of inactivity. Claim 21 contains the further requirement of taking the dose at a particular time to result in the avoidance of inhibitory activity during periods of intended sleep.

As noted above in WO88/08708, the only relevant teaching is of a sustained release capsule to maintain a constant level of active compound in the patient's blood stream. Moorman teaches the use of galanthamine in a controlled release formulation to treat nicotine dependence. Such controlled release is continuous (see column 1 line15, column 4 line 10) and active over a long period (column 4 line 38). The example in Moorman (Column 4, line 51-52 and Table 1) notes "The duration of application amounted to 24 hours." There is nothing in this teaching that would lead one to formulate a composition and choose its dosing time to provide periods in inactivity of galanthamine. The previous examiner made reference to Moorman's statement that galanthamine promotes awakening from twilight sleep

caused by scopolamine. As explained in response to the previous action, this is irrelevant to the present invention. Twilight sleep is a condition induced by scopolamine that has been used for sedation and the induction of amnesia for pain during labor and child birth. It has nothing to do with regular sleep. In any case, there is no suggestion that there should be periods in which galanthamine administered to a patient but deliberately remained inactive for a period after administration.

It is therefore submitted that Claims 1, 21 and 41, particularly as now amended, and the claims dependent on them meet the requirements of 35 USC 103(a).

New Claim 42 even more expressly ties the choice of inhibitor and composition to one that will produce a hypocholinergic effect during sleep and is also in no way suggested by any of the cited prior art.

Applicant submits that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted

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